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Neuroscience in China 2010–2011

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Over the past two years, there have been greater numbers of contributions made by Chinese scientists in various areas of neuroscience compared with the last 10 years, indicating the unprecedented rapid development of Chinese science. The research has related to various areas, including cellular and molecular neuroscience, developmental neuroscience, systems and computational neuroscience, mechanisms of neural disorders, and neuropharmacology in animal models.

Developmental neuroscience is always a "hot topic", where progress is helpful not only to the understanding of the formation of neural networks, but also towards the reconstruction of a deficient nervous system. The developmental regulation and isolation of neural stem/progenitor cells (NSPCs) and their functions in neurogenesis have been reviewed [1]. Unlike fetal brain, the persistence of neuroblasts in adult brain is controversial. Recently, evidence from adult monkey and human brains suggests that neuroblasts may be generated in the subventricular zone (SVZ) and then continuously migrate to the rostral migratory stream (RMS) [2]. Furthermore, Cheng et al. [3] found that newborn neurons in the dentate gyrus (DG) migrated to the inner part of the granule cell layer using a mouse model based on the Cre/loxp system, providing an efficient way to selectively label and manipulate newborn neurons in the adult mouse DG. However, the integration of newborn neurons into the existing circuit is difficult because of their poor survival, insufficient proliferation and differentiation abilities. A ciliary neurotrophic factor (CNTF)-collagen gel-controlled delivery system was found to provide a physical scaffold for the transplanted NSPCs to adhere to and migrate, as well as facilitating NSPCs survival, growth and proliferation, and simultaneously reducing the consumption of expensive growth factors [4]. Treatment with salvianolic acid B can also increase the number of neural stem cells (NSCs) and their derivative neurospheres, and promote the neurite outgrowth of NSCs and their differentiation into neurons [5].

Formation of the nervous system requires correct neuron functions, including axon guidance, neural migration [6], synaptic formation and remodeling [7], neural plasticity [8], glial cells [9], and neurite outgrowth. However, the precise neuroanatomical architecture remains unknown. A new tool for the mapping of neurite circuits at the mesoscale level, named micro-optical sectioning tomography, has been developed. It can provide a map in which the morphology and spatial locations of neurons and traces of neurites can be clearly distinguished, and was used to develop a 3D structural data set of a Golgi-stained whole mouse brain at the neurite level [10]. The strength of excitatory synaptic inputs in layer V pyramidal neurons of the medial prefrontal cortex were found to regulate social hierarchy in mice [11]. Myelination is another important part of neuronal development. In mice, the *Rheb1* transgene in neural progenitor cells increased mTORC1 activity and promoted myelination in the brain, indicating a crucial role for Rheb1 [12]. Glial cell line-derived neurotrophic factor (GDNF) activation of neurite outgrowth has been widely reported. Its negative regulation has been studied and Rap1GAP is reported to interact with RET to suppress GDNF-induced neurite outgrowth [13]. Lg11 activation of Rab10 promotes axonal membrane trafficking required for neuronal polarization [14]. *N*-cadherin-dependent interaction between neurons is required for maintaining the activity-induced growth of dendrites [15].

The importance of signal transduction and signaling pathways in the nervous system are self-evident. However, mechanisms involved in the release of neurotransmitters, transport of receptors and interactions between receptors are still unclear. Recently, one study found cross-talk between NMDA and $GABA_A$ receptors as well as Ca^{2+}/calmodulin-dependent protein kinases II in cultured neurons of the rat inferior colliculus, a central auditory system [16]. Another

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study observed large dense-core vesicles (LDCVs) transfer various GPCRs, ion channels and peptides in the dorsal spinal cord, enabling a rapid, activity-dependent modulation of neuronal sensitivity [17]. Interaction between μ- and δ-opioid receptors in nociceptive afferent neurons is involved in morphine analgesic tolerance [18,19]. Moreover, follistatin-like 1 secreted from nociceptive afferent terminals acts as an activator of presynaptic sodium pump and suppresses excitatory neurotransmission [20]. Furthermore, the formation, function and plasticity of sensory circuits are studied in the *Drosophila* by several groups [21–23]. Interestingly, neuregulin-ErbB4 signaling is found to contribute to the mechanism of epilepsy [24,25]. Neurodegenerative diseases have been widely studied in terms of the features described above [26]. Recent data has shown that the concentration of copper ions and formaldehyde are highly related to the pathology of Alzheimer's disease (AD) [27,28], and the investigation of ion channels in neuronal survival during the past 10 years in China was recently reviewed [29]. More evidence indicates that formaldehyde can not only promote Tau to form pore-like aggregates, but also induce hyperphosphorylation of Tau and disrupt its protection of DNA [30]. Furthermore, Su et al. [31] modified 2,4-dinitrophenylhydrazine (2,4-DNPH) method to analyze endogenous formaldehyde with higher sensitivity and lower relative standard deviations using UV-HPLC. All these studies improve the research about pathology of AD. In Huntington's disease, an important domain of huntingtin protein containing Htt4-17 was shown to regulate the cytoplasmic localization of this protein and impact on aggregate formation [32]. The mechanisms of PD related proteins, α-synuclein and Parkin for example, have been summarized [33]. Biomarkers for neural diseases remain to be improved. Currently, there is no specific biomarker for early-stage AD in the cerebrospinal fluid or blood [34]. Although recent studies indicated thiobarbituric acid reactive substances, nitric oxide, catalase (CAT) and glutathione peroxidase (GP) (molecules related to oxidative stress) may be biomarkers for schizophrenia, further study and confirmation is required [35]. Both attention deficit hyperactivity disorder (ADHD) and schizophrenia are related to the dysfunction of midbrain dopamine neurons. A study in mice demonstrated that the GC-C/PKG signaling pathway may be responsible [36]. Non-coding RNA (ncRNA) has recently received more attention and given plenty of research results. The role of ncRNA in pathophysiological mechanism in several neurodegenerative diseases has been reviewed [37]. Some other research studied the formation and process of memory and cognition [38–41], which may help us to understand the defection of cognition and memory in psychotic. More and more emphases are being laid on the studies of endophenotypes in neurodegenerative diseases [42–47].

Other studies have focused on drug usage and pharmacology especially in the central nervous system. The effective treatment of central nervous system disorders is limited by the blood brain barrier (BBB). A simple diffusion system proposed by Han et al. [48] has been validated and can deliver drugs effectively through bypassing the BBB. Fu et al. [49] identified a selective $GABA_B$ agonist, Baclofen, which can differentially modify cortical electroencephalography activity, elucidating the relationship between $GABA_B$ receptor-mediated neurotransmission and aging. Drug addiction is common in pain treatment. Recent studies of the mechanism of pain is popular and reviewed by Zhang [50]. A new study by Chen et al. [51] showed that endogenous encephalin may not be involved in the antihyperalgesic effects of gabapentin. The inflammation-induced afferent neurotransmission can be inhibited by activating B-Type natriuretic peptide signal pathway [52]. Moreover, intrathecal treatment of follistatin-like 1 could reduce chronic pain induced by nerve injury [53].

Computational neuroscience is an exciting new field that has developed over the last ten years, with multidisciplinary interactions including experimental neuroscience, robotics and computer vision [54]. The current review reports on the activity of rat pre-frontal cortex (PFC) neurons controlled by a one-dimensional (1D) machine using an encoding method to quench thirst [55]. This may benefit disabled patients. However, mature technology such as imageology plays important roles in other areas. For instance, high-resolution magic-angle spinning proton nuclear magnetic resonance spectroscopy and pattern recognition (HRMAS ^{1}H NMRS) are used in grade classification of neuroepithelial tumors according to metabolic fingerprints [56]. Based on number series completion, a typical data-driven scientific discovery task, the resulting data obtained by functional magnetic resonance imaging (fMRI) reveled the left dorsolateral prefrontal cortex (DLPFC) is related to rule identification, while the left anterior prefrontal cortex (APFC) may be involved in mental set maintenance needed during rule identification and extrapolation [57]. Furthermore, using fMRI-BOLD signals and ERP, Zhang et al. [58] indicated a bottom-up saliency map is created in V1, challenging the dominant view that the saliency map is generated in the parietal cortex.

In neuroscience studies, greater attention is being directed towards the development of animal models. Since the well-known genetic background and measurable cognitive behaviors, *Drosophila* has been widely used as an animal model for research in visual cognition and information processing in the perspective of genes-brain-behavior [59,60]. To understand the regulatory mechanisms of dendritic development, retinal ganglion cells (RGCs) of mice have been used [61]. Furthermore, the rat was also used in behavior studies such as the influence of social isolation [62]. Interestingly, an animal model for social hierarchy has been developed and used to analyze the neural circuits controlling the social behavior [11]. In addition to sleep and emotion, orexin plays a role in central vestibular motor control [63].

Despite amazing progress over the past few decades, the

nature of the nervous system remains unresolved. For example, the generation and survival of NSPCs, neuronal migration and plasticity, synaptic formation and shaping and the neural circuits underlying functions still require further study. Elucidation of these mysteries requires multidisciplinary combination at different levels. We look forward to greater contributions from Chinese neuroscientists in these areas.

1 Jiao J. Embryonic and adult neural stem cell research in China. Sci China Life Sci, 2010, 53: 338–341
2 Wang C, Liu F, Liu Y Y, et al. Identification and characterization of neuroblasts in the subventricular zone and rostral migratory stream of the adult human brain. Cell Res, 2011, 21: 1534–1550
3 Cheng X, Li Y, Huang Y, et al. Pulse labeling and long-term tracing of newborn neurons in the adult subgranular zone. Cell Res, 2011, 21: 338–349
4 Yang Z, Qiao H, Li X. Effects of the CNTF-collagen gel-controlled delivery system on rat neural stem/progenitor cells behavior. Sci China Life Sci, 2010, 53: 504–510
5 Guo G, Li B, Wang Y, et al. Effects of salvianolic acid B on proliferation, neurite outgrowth and differentiation of neural stem cells derived from the cerebral cortex of embryonic mice. Sci China Life Sci, 2010, 53: 653–662
6 Yuan X. Axon guidance and neuronal migration research in China. Sci China Life Sci, 2010, 53: 304–314
7 Luo Z. Synapse formation and remodeling. Sci China Life Sci, 2010, 53: 315–321
8 Zhang X, Poo M M. Progress in neural plasticity. Sci China Life Sci, 2010, 53: 322–329
9 Duan S. Progress in glial cell studies in some laboratories in China. Sci China Life Sci, 2010, 53: 330–337
10 Li A, Gong H, Zhang B, et al. Micro-optical sectioning tomography to obtain a high-resolution atlas of the mouse brain. Science, 2010, 330: 1404–1408
11 Wang F, Zhu J, Zhu H, et al. Bidirectional control of social hierarchy by synaptic efficacy in medial prefrontal cortex. Science, 2011, 334: 693–697
12 Zou J, Zhou L, Du X X, et al. Rheb1 is required for mTORC1 and myelination in postnatal brain development. Dev Cell, 2011, 20: 97–108
13 Jiao L, Zhang Y, Hu C, et al. Rap1GAP interacts with RET and suppresses GDNF-induced neurite outgrowth. Cell Res, 2011, 21: 327–337
14 Wang T, Liu Y, Xu X H, et al. Lgl1 activation of rab10 promotes axonal membrane trafficking underlying neuronal polarization. Dev Cell, 2011, 21: 431–444
15 Tan Z J, Peng Y, Song H L, et al. N-cadherin-dependent neuron-neuron interaction is required for the maintenance of activity-induced dendrite growth. Proc Natl Acad Sci USA, 2010, 107: 9873–9878
16 Cong D, Tang Z, Li L, et al. Cross-talk between NMDA and GABA(A) receptors in cultured neurons of the rat inferior colliculus. Sci China Life Sci, 2011, 54: 560–566
17 Zhao B, Wang H B, Lu Y J, et al. Transport of receptors, receptor signaling complexes and ion channels via neuropeptide-secretory vesicles. Cell Res, 2011, 21: 741–753
18 Wang H B, Zhao B, Zhong Y Q, et al. Coexpression of delta- and mu-opioid receptors in nociceptive sensory neurons. Proc Natl Acad Sci USA, 2010, 107: 13117–13122
19 He S Q, Zhang Z N, Guan J S, et al. Facilitation of mu-opioid receptor activity by preventing delta-opioid receptor-mediated codegradation. Neuron, 2011, 69: 120–131
20 Li K C, Zhang F X, Li C L, et al. Follistatin-like 1 suppresses sensory afferent transmission by activating Na^+, K^+-ATPase. Neuron, 2011, 69: 974–987
21 Hu A, Zhang W, Wang Z. Functional feedback from mushroom bodies to antennal lobes in the *Drosophila* olfactory pathway. Proc Natl Acad Sci USA, 2010, 107: 10262–10267
22 Huang J, Zhang W, Qiao W, et al. Functional connectivity and selective odor responses of excitatory local interneurons in *Drosophila* antennal lobe. Neuron, 2010, 67: 1021–1033
23 Gong Z, Liu J, Guo C, et al. Two pairs of neurons in the central brain control *Drosophila* innate light preference. Science, 2010, 330: 499–502
24 Li K X, Lu Y M, Xu Z H, et al. Neuregulin 1 regulates excitability of fast-spiking neurons through Kv1.1 and acts in epilepsy. Nat Neurosci, 2012, 15: 267–273
25 Tan G H, Liu Y Y, Hu X L, et al. Neuregulin 1 represses limbic epileptogenesis through ErbB4 in parvalbumin-expressing interneurons. Nat Neurosci, 2012, 15: 258–266
26 Zhou J. Recent progress in neurodegenerative disorder research in China. Sci China Life Sci, 2010, 53: 348–355
27 Luo Y, Zhang J, Liu N, et al. Copper ions influence the toxicity of beta-amyloid(1-42) in a concentration-dependent manner in a *Caenorhabditis elegans* model of Alzheimer's disease. Sci China Life Sci, 2011, 54: 527–534
28 He R, Lu J, Miao J. Formaldehyde stress. Sci China Life Sci, 2010, 53: 1399–1404
29 Wang Y, Xu T. Ion channels in neuronal survival. Sci China Life Sci, 2010, 53: 342–347
30 Lu J, Miao J Y, Pan R, et al. Formaldehyde-mediated hyperphosphorylation disturbs the interaction between Tau protein and DNA. Prog Biochem Biophys, 2011, 38: 1113–1120
31 Su T, Wei Y, He R Q. Assay of brain endogenous formaldehyde with 2,4-dinitrophenylhydrazine through UV-HPLC. Prog Biochem Biophys, 2011, 38: 1171–1177
32 Yan Y, Peng D, Tian J, et al. Essential sequence of the N-terminal cytoplasmic localization-related domain of huntingtin and its effect on huntingtin aggregates. Sci China Life Sci, 2011, 54: 342–350
33 Lu L, Gu L, Liang Y, et al. Dual effects of alpha-synuclein on neurotoxicity induced by low dosage of rotenone are dependent on exposure time in dopaminergic neuroblastoma cells. Sci China Life Sci, 2010, 53: 590–597
34 Zheng Y, He J, Hong T. Biomarkers of Alzheimer's disease in body fluids. Sci China Life Sci, 2010, 53: 490–496
35 Zhang M, Zhao Z, He L, et al. A meta-analysis of oxidative stress markers in schizophrenia. Sci China Life Sci, 2010, 53: 112–124
36 Gong R, Ding C, Hu J, et al. Role for the membrane receptor guanylyl cyclase-C in attention deficiency and hyperactive behavior. Science, 2011, 333: 1642–1646
37 Huang W T, Guo X Q, Dai J P, et al. MicroRNA and lncRNA in neurodegenerative diseases. Prog Biochem Biophys, 2010, 37: 826–833
38 Wang M, Geng H Y. The adaptive characteristics of memory: A perspective from the life-span development of associative memory illusion. Chin Sci Bull, 2010, 55: 1581–1589
39 Guo C Y, Chen W J, Tian T A, et al. Orientation to learning context modulates retrieval processing for unrecognized words. Chin Sci Bull, 2010, 55: 2966–2973
40 Wang X Z, Zhong N, Lu S F, et al. Parietal cortex contributions to information granules following memory consolidation. Chin Sci Bull, 2010, 55: 2671–2676
41 Zhang F, Geng H Y. What can false memory tell us about memory impairments in Alzheimer's disease? Chin Sci Bull, 2010, 55: 3989–3997
42 Chan R C K. Consortium for the Human Information and Neurocognitive Endophenotype (CHINE) in mainland China: An example from neurological soft signs for neuropsychiatric disorders. Chin Sci Bull, 2011, 56: 3409–3415
43 Chan R C K, Gottesman I I, Fu X L. Endophenotype strategies for the study of neuropsychiatric disorders: A quest. Chin Sci Bull, 2011, 56: 3359–3360
44 Glahn D C, Blangero J. Why endophenotype development requires families. Chin Sci Bull, 2011, 56: 3382–3384

45 Lui S S Y, Sham P, Chan R C K, et al. A family study of endophenotypes for psychosis within an early intervention programme in Hong Kong: Rationale and preliminary findings. Chin Sci Bull, 2011, 56: 3394–3397
46 Mcalonan G M, Yu K K, Chan R C K, et al. Is there an anatomical endophenotype for neurodevelopmental disorders? A review of dual disorder anatomical likelihood estimation (ALE) meta-analyses of grey matter volumes. Chin Sci Bull, 2011, 56: 3376–3381
47 Sham P C, Cherny S S, Hall M H. Statistical issues and approaches in endophenotype research. Chin Sci Bull, 2011, 56: 3403–3408
48 Han H, Xia Z, Chen H, et al. Simple diffusion delivery via brain interstitial route for the treatment of cerebral ischemia. Sci China Life Sci, 2011, 54: 235–239
49 Fu Y, Cui J, Ma Y. Differential effects of aging on EEG after baclofen administration. Sci China Life Sci, 2011, 54: 459–465
50 Zhang X. Pain research in China. Sci China Life Sci, 2010, 53: 356–362
51 Chen S, Zhao J, Huang Y, et al. Endogenous enkephalin does not contribute to the cerebral anti-hyperalgesic action of gabapentin. Sci China Life Sci, 2010, 53: 1428–1432
52 Zhang F X, Liu X J, Gong L Q, et al. Inhibition of inflammatory pain by activating B-type natriuretic peptide signal pathway in nociceptive sensory neurons. J Neurosci, 2010, 30: 10927–10938
53 Li K C, Wang F, Zhong Y Q, et al. Reduction of follistatin-like 1 in primary afferent neurons contributes to neuropathic pain hypersensitivity. Cell Res, 2011, 21: 697–699
54 Wu S, Liang P. Computational neuroscience in China. Sci China Life Sci, 2010, 53: 385–397
55 Lang Y, Du P, Shin H C. Encoding-based brain-computer interface controlled by non-motor area of rat brain. Sci China Life Sci, 2011, 54: 841–853
56 Chen W, Lou H, Zhang H, et al. Grade classification of neuroepithelial tumors using high-resolution magic-angle spinning proton nuclear magnetic resonance spectroscopy and pattern recognition. Sci China Life Sci, 2011, 54: 606–616
57 Zhong N, Liang P, Qin Y, et al. Neural substrates of data-driven scientific discovery: An fMRI study during performance of number series completion task. Sci China Life Sci, 2011, 54: 466–473
58 Zhang X, Li Z P, Zhou T, et al. Neural activities in v1 create a bottom-up saliency map. Neuron, 2012, 73: 183–192
59 Guo A, Zhang K, Peng Y, et al. Research progress on *Drosophila* visual cognition in China. Sci China Life Sci, 2010, 53: 374–384
60 Liang L, Luo L. The olfactory circuit of the fruit fly *Drosophila melanogaster*. Sci China Life Sci, 2010, 53: 472–484
61 Yang X, Shi X, He S. Properties of mouse retinal ganglion cell dendritic growth during postnatal development. Sci China Life Sci, 2010, 53: 669–676
62 Wen F, Xu L. Effects of isolation after sexual experience on anxiety-like, depressive-like behaviors and affective states in male rats. Chin Sci Bull, 2010, 55: 4136–4142
63 Zhang J, Li B, Yu L, et al. A role for orexin in central vestibular motor control. Neuron, 2011, 69: 793–804